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PROGRESS ON THE SYNTHESIS
OF EXTENDED PI SYSTEM
METALLOTETRABENZPORPHYRINS

BY

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A synthetic route to the fluorinated metalloporphyrin, zinc 1,2,3,4,5,6,10,11,12,13,14,18,19,20,21,22,25,26,27,28,29,30-tetracosafluoro tetranaphtho(1,2-b:1',2'-g:1'',2''-l:1''',2'''-q)porphyrin, was investigated. Diels-Alder reaction of tetrafluorobenzyne and N-trimethylsilylpyrrole, followed by catalytic hydrogenation and treatment with hydrochloric acid yielded tetrafluorobenzo-7-azanorbornene as the hydrochloride salt. However the same reaction sequence with hexafluoronaphthyne gave only a very low yield of hexafluoronaphtho-7-azanorbornene among other unidentified products. Intermediates and reaction products were characterized by infrared and nuclear magnetic resonance spectroscopy.

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PREFACE

The work described in this report was authorized under work unit number 1L161102AH5201019 entitled Energy Absorption and Dissipation Mechanisms in Organic Materials and covers the period from May 1986 to August 1986. The report describes the progress that was made on the synthesis of extended pi-system metallotetrabenzporphyrins during this period.

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METALLOTETRABENZPORPHYRINS

Introduction

The porphyrins and their metal complexes have been known for a long time and are of central importance in biological systems. The porphyrins, phthalocyanines and related compounds are of interest to the military because of their spectral properties. Porphyrin derivatives with the appropriate π-system should be able to be used as dyes that would be indistinguishable from natural background vegetation even by sophisticated spectrophotometric detection methods.

Although the simple porphyrins have been well characterized, there has been relatively little work done on porphyrin derivatives substituted with extended π-systems. This is due to the lack of good syntheses for such molecules. The first synthesis of a tetrabenzporphyrin (TBP) in reasonable yield was reported in 1978 by Vogler and Kunkely[1], who prepared zinc tetrabenzporphyrin, Zn TBP, (1a,R=H) in 17% yield by the reaction of 2-acetylbenzoic acid, zinc acetate and ammonia at 400°C. In 1981 Luk'yanets and coworkers reported another synthesis of metal TBP complexes.[2]

In 1983, D. Remy[3] of these laboratories reported a novel synthesis of tetrabenzporphyrins from isoindole.[4] Reaction of isoindole, zinc acetate and aldehydes at 375-400°C gave zinc TBPs in about 50% yield.

2a : Y-H

2b : X=F

1a : X=H

1b : X=F
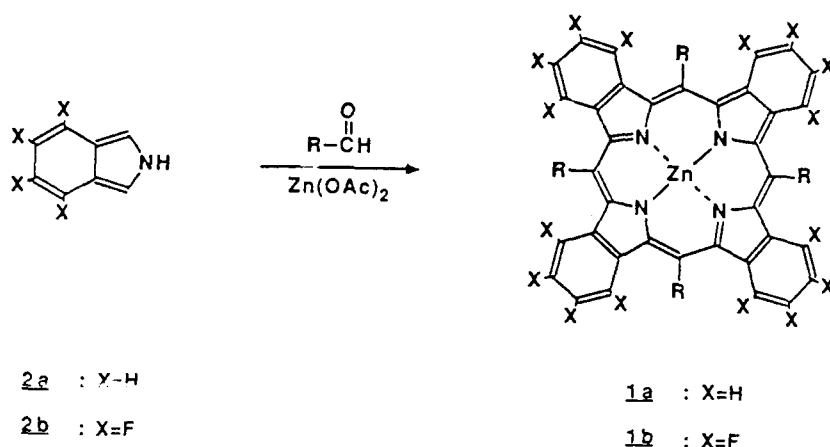
Not only did this method lead to the formation of the parent TBP (1a, R=H) in good yield, but it has also proved to be quite versatile in that a number of substituted TBPs have been prepared using the same procedure. For example, reaction of 4,5,6,7-tetrafluoisoindole (2b) with formaldehyde and zinc acetate gave zinc hexadecafluorotetrabenzporphyrin (1b, R=H).[3] In addition, it has been possible to prepare a number of meso-substituted TBPs (1a, R=Aryl) by reacting isoindole, zinc acetate, and various aromatic aldehydes.[5]

Molecules with even more extended π-systems are the analogous naphthoporphyrins. Luk'yanets and coworkers[6] have prepared the symmetrical tetra-2,3-naphthoporphyrin (3) from 3-oxo-2H-benz[f]isonindole-1-acetic acid. The isomeric tetra-1,2-naphthoporphyrin (4a) is an interesting molecule. In addition to the structure shown, which has C_{4h} symmetry, there are three other possible isomeric structures for tetra-1,2-naphthoporphyrin, each of which has a different symmetry. Luk'yanets and coworkers recently reported the synthesis of a
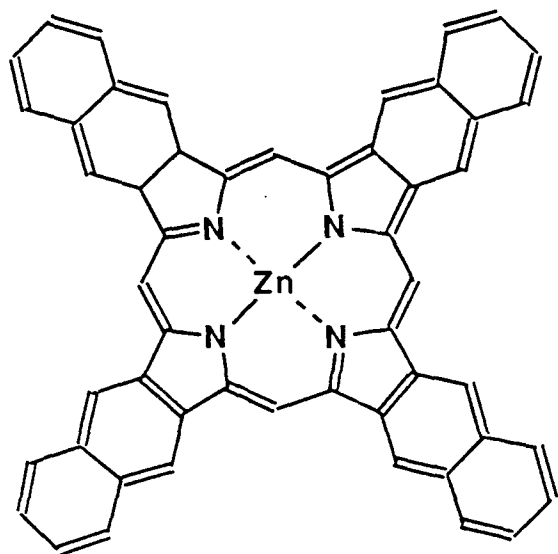
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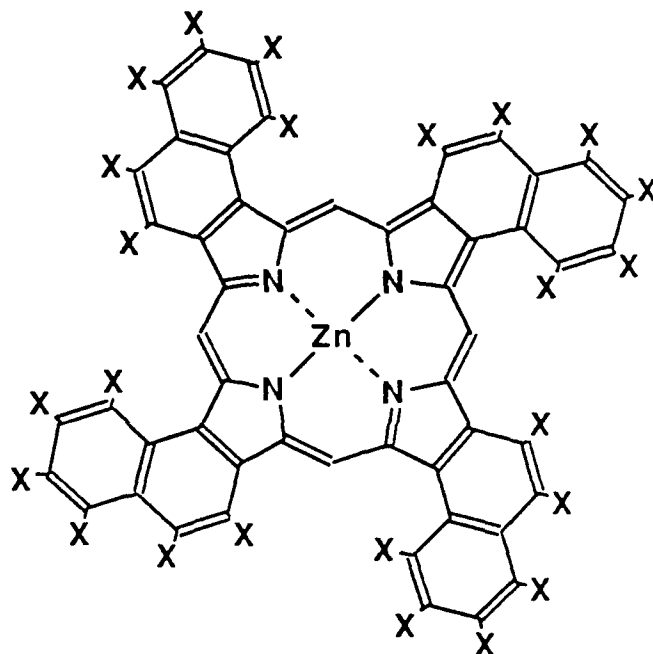
4a : X=H

4b : X=F

tetra-1,2-naphthoporphyrin from 3-(carboxymethyl)-5,6-benzophthal

imidine.[7] They assigned structure 4a with C_{4h} symmetry to their

compound, which was characterized only by elemental analysis and visible

spectrum. However a tetra-1,2-naphthoporphyrin was synthesized in these

laboratories recently from the reaction of benz[e]isoindole, formaldehyde,

and zinc acetate.[8] High resolution nuclear magnetic resonance (NMR)

indicates that the porphyrin formed from benz[e]isoindole is not the C_{4h}

isomer, in contrast with the results reported by the Russian workers.[7]

The goal of this project was to prepare the fluorinated analog of **4a**,
i.e., zinc 1,2,3,4,5,6,9,10,11,12,13,14,17,18,19,20,21,22,25,26,27,28,-
29,30-tetracosafluorotetranaphtho[1,2-b:1',2'-g:1''2''-1:1''',2'''-q]-
porphyrin (**4b**). This compound will complete a series of four compounds (**1a**,
1b, **4a** and **4b**) that will allow us to study systematically the effects of
substituting fluorine for hydrogen, and of extending the π-system of the
zinc tetrabenzporphyrin molecule, on its spectral and electrochemical
properties. In addition, it will be interesting to determine the
stereochemistry of the fluorinated material and to compare the results with
the hydrogen analog.

Results and Discussion

The proposed synthetic route to **4b** is shown in SCHEME I. A key step in
the sequence is the Diels-Alder reaction of hexafluoro-1,2-naphthyne (**10**)
and N-trimethylsilylpyrrole (**9**) to form the 7-azanorbornadiene ring system
of **11**. It has been shown that treatment of 2H-heptafluoronaphthalene with
n-butyllithium at low temperature generated hexafluoro-1,2-naphthyne (**10**)
(and not the 2,3-isomer), which reacts with furan to give a Diels-Alder
adduct.[9]

2H-heptafluoronaphthalene (**7**) was prepared in two steps from
octafluoronaphthalene (**5**).[10] Reaction of octafluoronaphthalene with
hydrazine in refluxing ethanol gave the β-substitution product, hepta-
fluoro-2-naphthylhydrazine (**6**). Reaction of **6** with Fehling's solution,
followed by steam distillation and sublimation, yielded 2H-heptafluoro-
naphthalene, m.p. 63-66°C (lit. 63-64.5°C). A mass spectrum showed the
product to be 95% heptafluorinated.

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SCHEME I
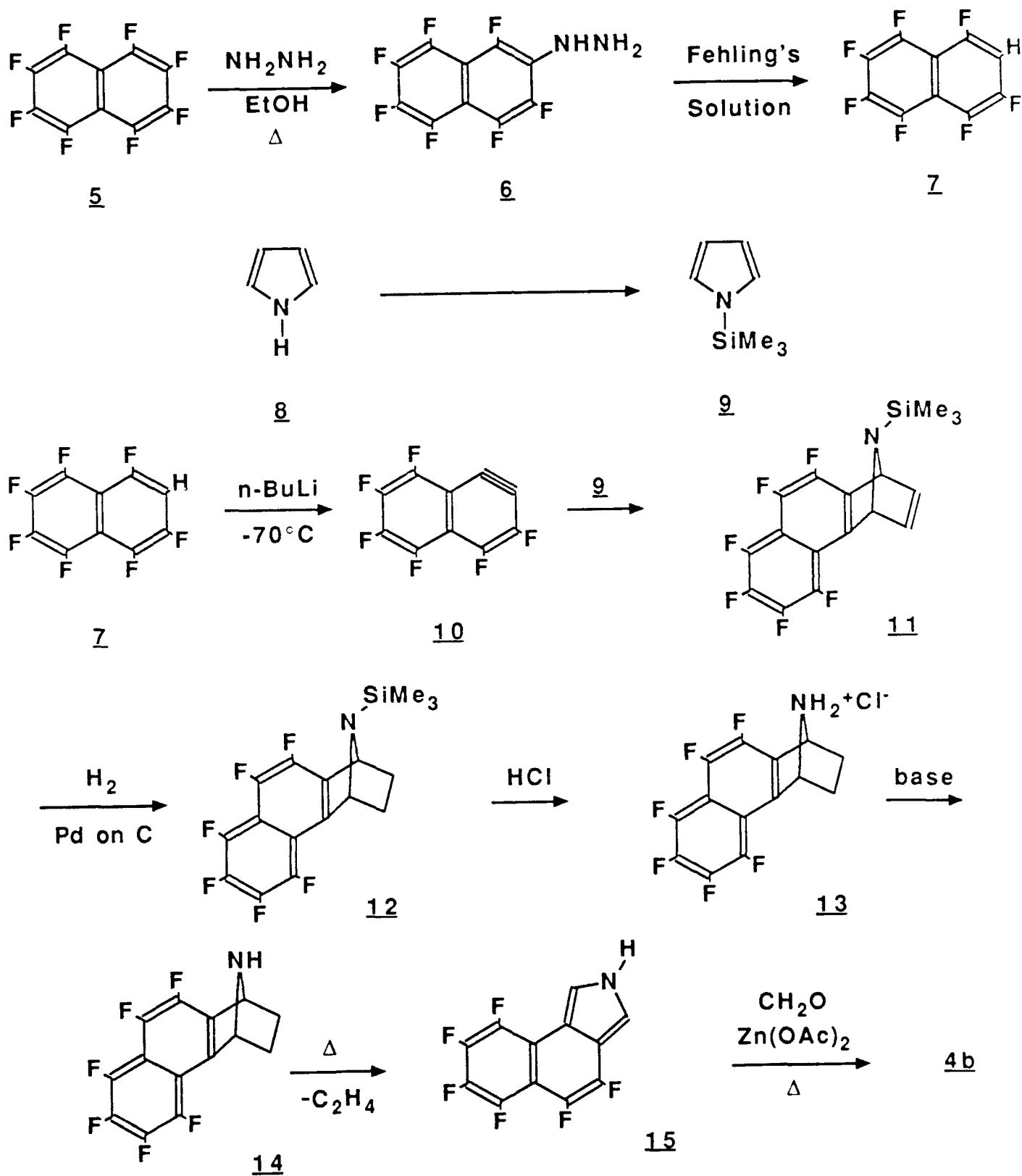
N-Trimethylsilylpyrrole ($\underline{9}$) was prepared from pyrrole ($\underline{8}$) using two different methods.[11] The first method was the reaction of pyrrole and potassium in refluxing dioxane to give potassium pyrrole followed by reaction with chlorotrimethylsilane. Distillation of the reaction mixture gave $\underline{9}$, b.p. 150-153°C (lit. 150-152°C). The product was characterized by the lack of an N-H stretching band at 3400 cm^{-1} in the IR spectrum and its 200 MHz proton NMR spectrum (CDCl$_3$): δ6.61 (s),2H, α-pyrryl; δ6.14 (s),2H, β-pyrryl; δ0.21 (s),9H, methyl.

N-Trimethylsilylpyrrole was also prepared by refluxing pyrrole and hexamethyldisilazane in the presence of a small amount of ammonium sulfate. This method proved to be superior to the first from the point of view of yield (60% vs 0-13%), length and difficulty of the procedure, and safety concerns.[12]

As a model for the sequence of reactions $\underline{10}$ --> $\underline{13}$ shown in SCHEME I, it was decided to run the analogous sequence on the tetrafluorobenzo series, $\underline{16}$ --> $\underline{20}$ (SCHEME II). This was done for several reasons. First, the procedure to make $\underline{7}$ is rather laborious and its supply was limited, whereas pentafluorobenzene ($\underline{16}$) is commercially available. Second, the greater symmetry of the tetrafluorobenzo series of compounds should greatly simplify the interpretation of NMR spectra. Third, $\underline{20}$ is useful as a precursor to zinc hexadecafluorotetrabenzporphyrin ($\underline{1b}$, R=H).

The reaction sequence $\underline{16}$ --> $\underline{20}$ was done without isolation of any of the intermediates. Pentafluorobenzene (1.68 g, 10.0 mmole) was added to 4.1 mL of 2.67M n-butyllithium (11.0 mmole) in diethyl ether (distilled from lithuim aluminum hydride) at -70°C under a nitrogen atmosphere. The tetrafluorobenzene solution was stirred at -70°C for 2 hours.

SCHEME II
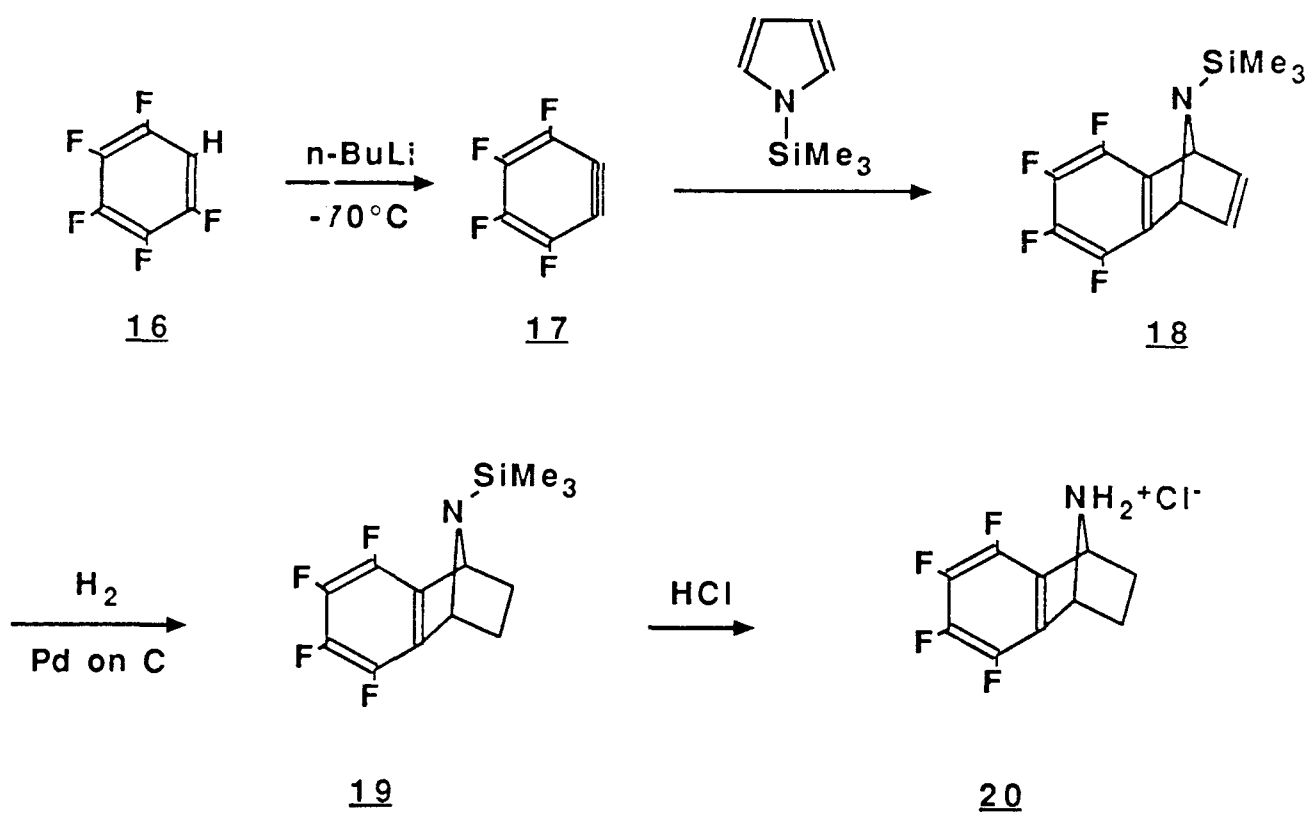
N-Trimethylsilylpyrrole (13.9 g, 10.0 mmole) was then added and the reaction mixture was warmed to room temperature and stirred overnight.[13] The ether solution was washed twice with deionized water and dried over anhydrous sodium sulfate. The ether solution containing the Diels-Alder adduct 18 was then immediately subjected to hydrogenation using a Parr hydrogenation apparatus and a small amount of 5% Pd-on-C as a catalyst. After filtering off the catalyst, hydrogen chloride gas was bubbled through the ether solution of 19 for 5 minutes to cleave the trimethylsilyl group. The light tan precipitate which formed was filtered and dried in vacuo to give 0.40 g (16% overall yield from 16) of the amine hydrochloride 20. The identity of 20 was confirmed by its proton NMR spectrum ($DMSO-d_6$): δ 10.2 (broad) 2H, NH; δ 5.63 (broad singlet), 2H, bridgeheads; δ 2.3 (m), 2H, exo H's; δ 1.60 (m), 2H, endo H's.

The Diels-Alder-hydrogenation-deprotection sequence was then applied to 2H-heptafluoronaphthalene. Treatment of 7 with n-butyllithium at -70°C, followed by addition of N-trimethylsilylpyrrole and treatment with hydrogen and 5% Pd-on-C, followed by treatment with HCl gas, gave a white solid that immediately became a brown oily solid on exposure to air, indicating that 13 or some other byproduct of the reaction sequence is very sensitive to air oxidation, hydrolysis, and/or polymerization. This material was shaken with a mixture of saturated aqueous $NaHCO_3$ and chloroform, and filtered. Thin layer chromatography of the chloroform extract indicated the presence of at least ten compounds. The chloroform extract was then subjected to column chromatography on silica gel. Gradient elution with hexane/chloroform gave 0.30 g of a brown oil. A proton NMR ($CDCl_3$) of this material showed that some of the desired amine 14 was present, but that it was a minor component of the sample.

Tentative NMR assignments for 14 are given below.

δ 3.12

H

δ 5.32

N

H H δ 2.22

F

F

H δ 1.29

F

H 'H δ 2.18

F

H H

H δ 1.25

F

F

δ 5.01

F
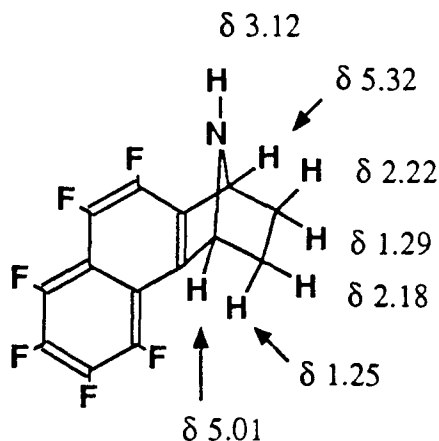
The failure of the reaction sequence to give the phenanthracene-1,4-imine 14 in reasonable yield was unfortunate and unexpected, especially in view of the ease of formation and isolation of the naphthalene-1,4-imine hydrochloride 20. The reason for the differences in reactivity between the two systems is unclear.

At this point the use of the trimethylsilyl protecting group was abandoned. Previously the N-benzyl analog of 12 has been prepared from N-benzylpyrrole. However, the removal of the benzyl group by hydrogenolysis was difficult and gave 15 in very low yield.[14] Therefore, it was decided to use the p-methoxybenzyl group to protect the nitrogen. Cleavage of this group to give 14 should occur under milder conditions and would hopefully form 14 in good yield.

N-(p-Methoxybenzyl) pyrrole has been reported[15] but has not been fully characterized. Addition of p-methoxybenzyl chloride to potassium pyrrole in dioxane followed by vacuum distillation afforded a colorless liquid whose infrared spectrum was consistent with the expected structure.

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The proton NMR spectrum (CDCl$_3$) confirmed the formation of N-(p-methoxy-benzyl) pyrrole: δ7.00 (d) and 6.80 (d), 4H, Ar-H; δ6.61 (s), 2H, α-pyrryl; δ6.14 (s), 2H, β-pyrryl; δ4.91 (s), 2H, CH$_2$; δ3.70 (s), 3H, OCH$_3$.

Conclusions

In an ongoing effort to examine the spectral and electrochemical properties and potential catalytic activity of porphyrins with extended π-systems, a synthetic route to the fluorinated 1,2-naphthoporphyrin 4b was investigated. The synthesis involved Diels-Alder addition of hexafluoro-1,2-naphthyne to N-trimethylsilylpyrrole, followed by hydrogenation of the olefinic double bond and removal of the trimethysilyl protecting group to generate the phenanthrene-1,4-imine 14. Retro Diels-Alder reaction of 14 would produce hexafluorobenz[e]isoindole 15, which should form the porphyrin 4b on heating with zinc acetate and paraformaldehyde.

The Diels-Alder-hydrogenation-deprotection sequence worked in the case of the benzo series and 20 was obtained in reasonable yield. However, in the 1,2-naphtho series, the same reaction sequence gave 14 in very low yield.

p-Methoxybenzylpyrrole has been synthesized and characterized. The p-methoxybenzl group may be a superior blocking group for the pyrrole nitrogen atom in that its removal should be effected under milder conditions than the trimethylsilyl or benzyl group. It is, therefore, recommended that synthetic efforts on this project be focused on the p-methoxybenzyl series of compounds which should lead to more facile synthesis of the phenanthrene-1,4-imine 14.

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